Claims

We claim:

Claim 1. A library of structurally-constrained peptides comprising a plurality of cyclic peptides, wherein each said cyclic peptide comprises an amino acid sequence C1-A1-A2-$(A3)_n$-A4-A5-C2 [SEQ ID NO: 1],

wherein

A1, A2, A3, A4, and A5 are naturally occurring L-amino acids;

the carboxy terminus of Cysteine C1 is optionally protected with a carboxy protecting group;

the amino terminus of Cysteine C2 is optionally protected with an amino protecting group;

A1 and A5 are selected from the group consisting of amino acids W, Y, F, H, I, V and T;

A2 and A4 are selected from the group consisting of amino acids W, Y, F, L, M, I, and V;

A3 is any naturally occurring L-amino acid and n is an integer that is 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12; and

C1 and C2 are joined together by a disulfide bond thereby forming a cyclic peptide.

Claim 2. The library of claim 1, wherein A1 or A5 is a β-branched residue having two non-hydrogen substituents on the β-carbon of the amino acid residue.

Claim 3. The library of claim 1, wherein A1 or A5 is T.

Claim 4. The library of claim 1, wherein A1 or A5 is amino acid W, F, H or Y.

Claim 5. The library of claim 1, wherein A2 or A4 is amino acid W, F or Y.

Claim 6. The library of claim 5, wherein A2 or A4 is W.

Claim 7. The library of claim 6, wherein A2 and A4 are W.

Claim 8. The library of claim 1, wherein n is at least 4.

Claim 9. The library of claim 8, wherein n is no greater than 10.

Claim 10. The library of claim 9, wherein n is 4.

Claim 11. The library of claim 10, wherein $(A3)_4$ is EGNK, ENGK, QGSF or VWQL.

Claim 12. The library of claim 11, wherein A1 is T and A5 is T.

Claim 13. The library of claim 12, wherein A2 is W or L.

Claim 14. The library of claim 13, wherein A4 is W or L.

Claim 15. The library of claim 1, wherein the cyclic peptide is fused to at least a portion of a phage coat protein, and the cyclic peptide is displayed on the surface of a phage or phagemid particle.

Claim 16. A method of screening for peptides having a β-hairpin scaffold that is conformationally stabilized, comprising the steps of:

a) providing a library of claim 1;
b) selecting at least two peptides from the library of step a), wherein said at least two peptides differ by one amino acid at a particular position A1, A2, A3, A4 or A5;
c) determining the conformations of the peptides of step b);
d) measuring and comparing the relative free energies of the peptides of step b);
e) selecting peptides having a conformationally stabilized β-hairpin scaffold.

Claim 17. A method of identifying a peptide capable of binding to a specific binding partner, comprising the steps of:

a) providing a library of claim 1;
b) contacting the library of step a) with a binding partner;
c) selecting from the library peptides capable of forming a noncovalent complex with the binding partner; and
d) optionally isolating the peptides of step c).

Claim 18. The method of claim 17, wherein the binding partner is selected from the group consisting of an antigen, an antibody, an enzyme, an enzyme substrate, a receptor and a ligand.